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APPLICANT:	**PORTER, Thomas R.**	ART UNIT: 1619
SERIAL NO:	(cont. of 09/435,050)	EXAMINER: Harrison, R.
FILED:		
TITLE:	**THROMBOLYTIC AGENTS AND METHODS OF TREATMENT FOR THROMBOSIS**	

PRELIMINARY AMENDMENT

Commissioner of Patents and Trademarks
Washington, D.C. 20231

Dear Sir:

Please enter the following amendment into the record.

IN THE SPECIFICATION

Before the "Background of the Invention", please insert the following:

--CROSS REFERENCE TO A RELATED APPLICATION

This application is a continuation of Serial Number 09/435,050 filed November 8, 1999, which is a continuation of Serial Number 08/832,532 filed April 3, 1997, which is a divisional of Serial Number 08/544,204 filed October 17, 1995, now U.S. Patent No. 5,648,098.--

CERTIFICATE OF MAILING (37 C.F.R. § 1.8(a))

I hereby certify this document and the documents referred to as enclosed therein are being deposited with the United States Postal Service in an envelope as "Express Mail Post Office to Addressee" addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 prior to 5:00 p.m. on the 11 day of January, 2001.

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IN THE CLAIMS

Please cancel claims 1-52.

Please add new claims 53-78.

53.

A method of mechanicaly dissolving thrombi in an animal comprising:

introducing a pharmaceutical composition to an animal by intravenous injection to a particular site where coagulation is desired to be minimized, said pharmaceutical composition comprising a microbubble ultrasound contrast agent, and thereafter;

applying ultrasound to said site.

54.

The method of claim 53 wherein said microbubble contrast agent comprises:

a plurality of gas filled microbubbles with a diameter of from about .1 to 10 microns.

55.

The method of claim 54 wherein said gas is an insoluble gas.

56.

The method of claim 54 wherein said microbubbles are protein coated.

57.

The method of claim 53 wherein said carrier is a 5% solution of dextrose.

58.

The method of claim 55 wherein said protein coated microbubbles are albumin coated microspheres.

59.

The method of claim 54 wherein said insoluble gas is selected from the group consisting perfluoromethane, perfluoroethane, perfluoropropane, perfluorobutane, and perfluoropentane.

60.

The method of claim 59 wherein said perfluorocarbon gas is perfluorobutane.

61.

The method of claim 59 wherein said perfluorocarbon gas is perfluoropropane.

62.

The method of claim 53 further comprising the following steps:

mixing an aqueous solution comprising 2% to about 10% by weight of human serum albumin diluted about 2-fold to about 8-fold with 5% to 50% by weight dextrose; and

exposing said solution to a sonication horn to generate stable microbubbles from about .1 to 10 microns in diameter to create said pharmaceutical composition.

63.

The method of claim 62 wherein said dilution of albumin with dextrose is a 3-fold dilution.

64.

The method of claim 62 wherein said human serum albumin is a 5% by weight solution.

65.

The method of claim 62 wherein said dextrose is a 5% by weight solution.

66.

A method of relieving trauma associated with obstruction of smaller vessels distal to a thrombus site by increasing

blood flow with or without thrombus dissolution and recanalization in animals comprising:

introducing a pharmaceutical composition to an animal with a thrombus by intravenous injection, said pharmaceutical composition comprising a microbubble ultrasound agent, and thereafter;

applying ultrasound to the area of trauma.

67.

The method of claim 66 wherein said microbubble contrast agent comprises:

a plurality of gas filled microbubbles with a diameter of from about .1 to 10 microns.

68.

The method of claim 67 wherein said gas is an insoluble gas.

69.

The method of claim 67 wherein said microbubbles are protein coated.

70.

The method of claim 66 wherein said carrier is a 5% solution of dextrose.

71.

The method of claim 68 wherein said protein coated microbubbles are albumin coated microspheres.

72.

The method of claim 67 wherein said insoluble gas is selected from the group consisting perfluoromethane, perfluoroethane, perfluoropropane, perfluorobutane, and perfluoropentane.

73.

The method of claim 72 wherein said perfluorocarbon gas is perfluorobutane.

74.

The method of claim 72 wherein said perfluorocarbon gas is perfluoropropane.

75.

The method of claim 67 further comprising the following steps:

mixing an aqueous solution comprising 2% to about 10% by weight of human serum albumin diluted about 2-fold to about 8-fold with 5% to 50% by weight dextrose; and

exposing said solution to a sonication horn to generate stable microbubbles from about .1 to 10 microns in diameter to create said pharmaceutical composition.

76.

The method of claim 75 wherein said dilution of albumin with dextrose is a 3-fold dilution.

77.

The method of claim 75 wherein said human serum albumin is a 5% by weight solution.

78.

The method of claim 75 wherein said dextrose is a 5% by weight solution.

REMARKS

Applicant is submitting new claims 53 and 78 which are directed to a method of discouraging blood clotting to induce thrombolysis in an animal and a method of relieving trauma associated with obstruction of smaller vessels in animals, respectively. Literal support for the subject matter of these claims is found on p. 1 of the specification wherein it states that "[t]he methods and composition of the invention can be used as an anticoagulant therapy to induce thrombolysis and to relieve trauma associated with obstruction of smaller vessels." No new matter has been added.

Applicant respectfully requests consideration of these claims.

Respectfully submitted,

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